



## Thoracoscopic sympathectomy is a valuable addition in the management of recreational intra-arterial drug injection. Pilot study

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### ABSTRACT

**Background:** Intra-arterial Injection (IAI) of illicit substances by drug abusers may result in acute ischemia, limb loss or permanent functional deficit. No prospective human studies have shown that any specific treatment is superior to another. Thoracoscopic sympathectomy (TS) has proven efficacy in upper limb ischemia due to organic blockade. This is a pilot study to evaluate the effect of thoracoscopic sympathectomy addition to the management protocol of recreational intra-arterial drug injection.

**Patients and methods:** A total of 11 victims of upper limb IAI of recreational drug were recruited (10 males) with age range from 18 to 43 years old (average  $30 \pm 8.3$  years). Tissue Ischemia Score (TIS) was used for pretreatment assessment of the degree of ischemic injury and severity of pain was evaluated pre- and post-operatively using visual analog score (VAS) and compared using Student's *t* test. Pre-operative VAS score was  $6.9 \pm 1.8$ . All enrolled patients were treated according to the following protocol; anticoagulation, calcium channel blocker, opiates for pain, and TS. Patients received the stated protocol for minimum of 72 h (range 3–8 days; mean 5; average  $4.7 \pm 1.5$  days). Freedom of amputation and improvement of pain scores were the study endpoints.

**Results:** No mortality, yet one case had bleeding secondary to anticoagulant and one case of post-operative pneumothorax that required chest tube drainage for 24 h. No patients had wet gangrene or spreading infection. Freedom of amputation was achieved in nine patients, 81% (7 patients had normal outcome and other two had permanent neurological deficit). Two patients (18%) had tissue necrosis with dry gangrene and mummification of the affected digits with eventual amputation. Postoperative VAS pain score was  $2.09 \pm 1.37$  ( $p < 0.05$ ). Pain medications were suspended in 6 patients (54.5%), reduced in 4 (36%) and unchanged in 1 (9%). All patients with TIS score 2 or less had a normal outcome while those with scores 3 and 4 had a variable outcome. Using regression analysis, initial TIS was significant for outcome prediction ( $p = 0.043$ ) while age, arterial site, drug injected and time delay were not significant.

**Conclusion:** The addition of TS was an attempt to halt the ischemic process after IAI which permitted, in our belief, optimal symptom control with maximum tissue salvage. Because the procedure is minimally invasive, safe, and associated with a low complication rate; it worth consideration whenever IAI is encountered.

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### 1. Introduction

Recreational drug abuse represents an increasing problem over the last two decades with estimated 13.5 million drug abuser world wide.<sup>1</sup> Unintentional intra-arterial injection (IAI) of illicit substances by drug abusers may result in catastrophic complications manifested by acute severe extremity ischemia with tissue necrosis and permanent neurological dysfunction.<sup>2</sup> The mechanisms of injury and

opportunities for treatment are different for IAI occurring in a hospital and that resulting from substance abuse. Iatrogenic IAI frequently involves a single drug with no impurities, is usually diagnosed immediately, and treatment may be initiated before the vascular injury has fully developed.<sup>3</sup>

In contrast, IAI by addicts may involve multiple substances that are invariably contaminated with impurities with frequent delay from injection to treatment, allowing the ischemic injury to develop.<sup>3,4</sup> Therefore the usual excellent results reported in the prompt treatment of iatrogenic IAI may not be possible in cases of drug abuse.<sup>3–6</sup> The advent of ischemia has a multifactorial origin and can be dependent on site of injection, the physicochemical

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drug properties and volume of the injected drug. Furthermore, various pathophysiological responses come into play; direct toxic effect of the drug producing chemical endarteritis resulting in endothelial injury, platelet activation and associated localized thrombosis.<sup>7,8</sup>

Since the first report of IAI by Van Der Post in 1942,<sup>9</sup> a variety of therapeutic modalities have been attempted to halt the ischemic process. However, guidelines regarding its management remain vague.<sup>10,11</sup> Most of the studies reported small number of patients with inadequate follow up, that would not culminate to evidence based recommendations regarding any treatment protocol.<sup>10–15</sup>

Palmar and axillopalmar hyperhidrosis represents the commonest indications for dorsal sympathectomy,<sup>16</sup> however, vascular insufficiency of the upper extremities, when revascularization is not feasible, represents a less common indication; which induces the release of vasomotor control and hyperactive tone of the small arteries and arterioles, improving circulation to the skin, peripheral extremities, and bone, allowing healing of ulcers and trophic lesions and limiting tissue necrosis.<sup>16,17</sup>

The minimal invasiveness of thoracoscopic sympathectomy had led many authors, in the past two decades, to re-examine the role of sympathectomy in intractable hand ischemia, however, only three reports (total of 7 patients) had reported its use in IAI sitting.<sup>18–20</sup>

This is a study to evaluate the effect of thoracoscopic sympathectomy addition to the management protocol of recreational intra-arterial drug injection.

## 2. Materials and methods

After obtaining the approval of Department of surgery's ethical committee on October 2005 victims of upper limb intra-arterial injection (IAI) of recreational drug were recruited to study the effect of thoracoscopic sympathectomy (TS) on their outcome, during the period from January 2006 to May 2009 at Cairo University Hospitals. Exclusion criteria included evidence of infective endocarditis, previous IAI at the same limb in question, American Society of Anesthesiology (ASA) class III and those presenting late with established tissue necrosis (dry gangrene). The nature of the procedure and the potential merits as a method under study was explained to each patient and a written informed consent was obtained.

A total of 11 patients (10 males and one female) with age range from 18 to 43 years old (average  $30 \pm 8.3$  years) were recruited (Table 1). Heroin was the most injected substance (63.4%), while radial artery was the most frequently injected site (5 patients). All patients gave a history of intense unrelenting pain immediately following injection with variable degrees of persistent pain afterwards. Their main presentations were pain, numbness, swelling, coldness and weakness. On examination all extremities showed

temperature loss and swelling distal to the injection site. Abnormal coolness or cold extremity was observed in 10 (90%) while cyanosis in 8 (72%). Seven patient (64%) had sensory deficit and 4 (36%) had motor deficit. Capillary refill was delayed  $>3$  s in 5 patients (45%). All patients had normal or even accentuated pulses at the wrist except one patient with ulnar artery injection had lost his ulnar pulse.

Tissue Ischemia Score (TIS) devised by Treiman et al., in 1990<sup>21</sup> was used for pretreatment assessment of the degree of ischemic injury. It reflects finding on initial physical examination that are most indicative of ischemic injury. It measures four parameters (cyanosis, coldness, delayed capillary refilling and neurological deficit) and it scores 0 for its absence and 1 for its presence. The sum of the values equal the TIS, therefore, it ranges from 0 (normal) and 4 (severe injury). Severity of pain was evaluated pre-and post-operatively using visual analog score (VAS), a numeric rating scale from 0 to 10 (0 = no pain; 1–3 = mild to moderate pain; 4–7 = severe pain and  $>8$  agonizing pain) and compared using Student's *t* test. Pre-operative VAS score, expressed as mean  $\pm$  standard deviation, was  $6.9 \pm 1.8$ .

All enrolled patients were treated according to the following protocol: (1) systemic anticoagulation (Enoxparine<sup>®</sup> at 1 mg/kg every 12 h SQ) after initial dose of IV sodium heparin at 80 IU/kg; (2) calcium channel blocker (Verapamil 80 mg PO, TID); (3) opiates for pain control; (4) adequate hydration with intravenous fluids and (5) thoracoscopic sympathectomy on next morning list basis. The affected extremity was elevated, and early physiotherapy was initiated with active and passive range of motions. Broad spectrum antibiotics were added in case of suspected or overt infection.

Thoracoscopic sympathectomy was performed by dual port, posterior approach technique,<sup>22,23</sup> under general anesthesia using single lumen tracheal intubation in prone position with sternal and pelvic support. After manual induction of pneumothorax, a 10 mm visual port was inserted at the 5th intercostal space at posterior axillary line and another 5 mm working port at 4th intercostal space 5–7 cm medial to the visual port with CO<sub>2</sub> inflation pressure of 5–7 mmHg. Dorsal sympathetic chain from T2 to T4 was excised by electrocautery hook on the affected side. At the end of the procedure the lung on the operative side was allowed to inflate by the help of Valsalva's like maneuver performed by the anesthetist and lung expansion was visually inspected with no need for routine chest tube drainage. All sympathectomy procedures went uneventfully except one case required chest tube drainage 6 h post-operatively and was removed 24 h later.

Indications for hand and/or forearm fasciotomy were excessive swelling not responding to proper limb elevation, tense compartmental boundaries and pain on passive movement of the compartment's muscles. None of our patients required fasciotomy in their management.

**Table 1**  
Patients' demographics, presentations and outcome.

No.	Age	Sex	Drug	Artery	Time delay	Wrist pulse deficit	Motor deficit	Cyanosis	Coldness	Delayed capillary refill	Sensory deficit	TIS	Outcome	Time to outcome (d)
1	42	M	Tr	Brach.	24	–	–	+	–	–	–	1	Nr	3
2	39	M	Roh	Brach.	36	–	–	+	+	–	+	3	Nr	5
3	18	M	Her	Rad	36	–	–	+	+	+	+	4	ND	4
4	22	M	Her	Rad	24	–	+	–	+	+	+	3	Nr	5
5	20	M	Her	Ulnar	16	+	+	+	+	+	+	4	TL	6
6	25	M	Her	Brach	40	–	+	+	+	+	+	3	Nr	5
7	31	M	Roh	Rad	18	–	–	–	+	–	–	1	Nr	3
8	40	M	Her	Rad	24	–	+	+	+	–	+	3	ND	6
9	29	M	Her	Ulnar	24	–	–	+	+	+	+	4	TL	8
10	28	F	Tr	Brach	32	–	–	+	+	–	–	2	Nr	3
11	36	M	Her	Rad	16	–	–	–	+	+	–	2	Nr	4

Her = heroin, Roh = rohypnol (Flunitrazepam), Tr = tramadol, Brach = brachial, Rad = radial, Nr = normal, ND = neurological deficit, and TL = tissue loss.

Patients received the stated protocol for a minimum of 72 h (range 3–8 days; mean 5; average  $4.7 \pm 1.5$  days). Freedom of amputation and improvement of pain scores were the study endpoints, freedom of amputation included patients with complete resolution of symptoms with a normal extremity and those with stable functional neurological deficit with intact extremity.

### 3. Results

No mortality occurred in the study, yet one patient with ulcer history had upper GI bleeding secondary to anticoagulant, which responded to medical management and another patient of post-operative pneumothorax that required chest tube drainage for 24 h with no further morbidity. No Horner's syndrome or other collateral effects were reported. No patients had wet gangrene or spreading infection that required urgent debridement or amputation.

After treatment, freedom of amputation was achieved in nine patients, 81% (7 patients had normal outcome and other two had permanent neurological deficit with intact extremity in the form of hand contracture and weak grip in one case and inability to flex two fingers in the other). Two patients (18%) had tissue necrosis with dry gangrene and mummification of the affected digits; eventually they required amputation of their finger tips.

Post-operative VAS pain score was  $2.09 \pm 1.37$  and the improvement from the preoperative values was statistically significant ( $p < 0.05$ ). Pain medications were suspended in 6 patients (54.5%), reduced in 4 (36%) and unchanged in 1 (9%) (Fig. 1).

All patients with TIS score 2 or less had a normal outcome while those with scores 3 and 4 had a variable outcome. Three out of four patients with TIS 3 had a normal outcome and only one patient had a viable extremity yet with neurological deficit. The situation was even worst for patients with TIS 4 where none had normal outcome and two out of three required eventually amputation to their finger tips due to dry gangrene and mummification.

Using regression analysis, initial TIS was significant for outcome prediction ( $p = 0.043$ ) while age, arterial site, drug injected and time delay were not significant.

### 4. Discussion

Case reports and incidences of iatrogenic intra-arterial injection (IAI) of medications have been published since the 1940s.<sup>24–26</sup> During the past few decades, the source of the problem has shifted from primarily hospitalized patients to people who abuse IV drugs. Additionally, the number of implicated medications has increased from a few sedatives to a much larger and diverse group of substances.<sup>21</sup>

A variety of theories have been proposed to explain the development of tissue necrosis from IAI; direct toxicity of the injected

drug to the vascular endothelium,<sup>27</sup> particulate emboli, altered pH with crystal formation,<sup>28</sup> increased platelet aggregation,<sup>7</sup> thromboxane release,<sup>29</sup> and increased sympathetic discharge of norepinephrine with vasospasm.<sup>30</sup>

Because of the incomplete understanding of the underlying pathophysiology and the impracticality of performing case controlled, prospective human studies, specific treatment algorithms have not been well developed.<sup>31</sup> Many therapeutic interventions have been attempted with varying degrees of success. Most interventions are largely empirical, aiming to maintain perfusion distal to the site of injury. No prospective human studies have shown that any specific treatment is superior to another.<sup>8,31</sup>

The implementation of sympathectomy in the management of peripheral ischemia is not a new concept.<sup>32,33</sup> Many reports in the literature examined the efficacy of sympathectomy for treating gangrene and ulcers due to occlusive arteriosclerosis of lower and upper limb arteries with variable results.<sup>34,35</sup> Thoracic sympathectomy has been performed for occlusive and vasospastic small arterial disease of upper extremity for several decades with mixed results.<sup>32–37</sup> Most series have found recurrence of symptoms after an initial period of improvement, especially in patients with vasospastic Raynaud's syndrome.<sup>35</sup> However, in a clear subset of patients with organic blockage of the distal vasculature resulting in terminal digital necrosis, gangrene, and significant pain at rest, TS has been found to be a valuable therapeutic option.<sup>36,37</sup>

Pain control, ulcer healing, and demarcation of necrosis appear to be much more related to postsurgical correction of abnormal arteriovenous shunting and to improved nutritional blood flow to ischemic areas than to the increase of total blood flow.<sup>38</sup> Recently, sympathectomy was proved to increase the blood flow by 66%, decrease the exercise pressor response and increase exercise tolerance by 150% due to its positive effect on skeletal muscles bioenergetics.<sup>39</sup>

Development of TS has made sympathectomy for the upper limb safe and minimally invasive. This has resulted in the procedure being done widely, especially for palmar hyperhidrosis.<sup>19</sup> A recent meta-analysis of all published literature confirms TS to be safe with very low morbidity.<sup>40,41</sup> In this study only one case developed pneumothorax with no hemothorax or Horner syndrome.

Numerous reports in the literature had addressed the role of sympathectomy in the sitting of limb ischemia, yet only three reports had reported the use of thoracoscopic sympathectomy in IAI among other causes of upper limb ischemia.<sup>18–20</sup> Only seven patients were reported collectively, in these series, with variable results. De Giacomo et al.,<sup>18</sup> reported three IAI patients, among 15 patients with upper limb ischemia, with more than 66% normal extremity outcome, Modagheh et al.,<sup>19</sup> reported also three IAI patients among 33 patients with full recovery in 31 patients, yet he did not specify the results in particular to IAI while Becquemin et al.,<sup>20</sup> reported one case of failure of sympathectomy to halt the progression of finger gangrene after incident of IAI. To our knowledge, to date, no study has been exclusively dedicated to evaluate the role of sympathectomy in IAI.

In this study thoracoscopic sympathectomy and medical treatment provided effective pain control (10/11) with satisfactory hand salvagability (9/11), even when amputation was necessary, it was delayed until a clear demarcation of necrosis was obtained, allowing the preservation of the maximal viable tissue. TIS proved to be a valuable prognostic tool with good prediction to outcome.

### 5. Conclusion

Because of the infrequent occurrence IAI, it is unlikely that any single institution will encounter enough patients to be able to randomize therapies and incorporate adequate controls to prove

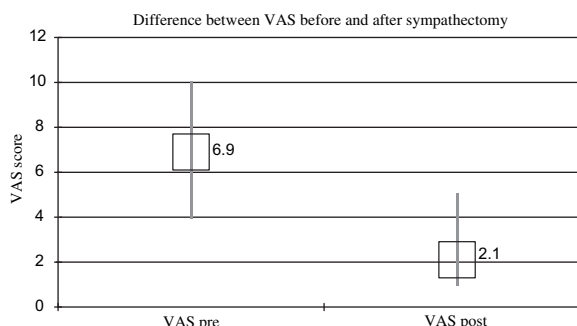


Fig. 1. VAS score pre and post-operative.

conclusively superiority of a given treatment protocol. However, the addition of TS was an attempt to halt the ischemic process after IAI which permitted, in our belief, optimal symptom control with maximum tissue salvage. Because the procedure is minimally invasive, safe, and associated with a low complication rate; it worth consideration whenever IAI is encountered.

#### Conflict of interest statement

None to declare.

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None.

#### Ethical approval

General surgery department ethical committee, October 2005.

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